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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/828,607	04/06/2001	Slobodan Vukicevic	STK/070	5821

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EXAMINER
ROBINSON, HOPE A

ART UNIT	PAPER NUMBER
1653	6

DATE MAILED: 05/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/828,607	VUKICEVIC ET AL.	
	Examiner	Art Unit	
	Hope A. Robinson	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-60* is/are pending in the application.

4a) Of the above claim(s) *35-46 and 51-56* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-34,47-50 and 57-60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's election with traverse of Group I (claims 1-34, SEQ ID NO: 6) in Paper No. 9 is acknowledged. The traversal is on the ground(s) that the claims not be restricted as set forth in Paper No .4 and that Groups I and III be examined together because applicant asserts that there is no serious burden for the examiner to search as these searches overlap. Note that Groups I and III have been rejoined as requested because a search of the claimed invention produced references that teach the subject matter of both groups.

The traversal is also on the ground(s) that the claims not be restricted to one sequence because applicant asserts that claim 1 is a linking claim which links sequences contained in SEQ ID NOS: 3-7. This is not found persuasive because the claimed sequences set forth in SEQ ID NOS: 3-7 are structurally distinct, representing different osteogenic proteins (see for example the sequence listing).

The requirement is still deemed proper and is therefore made FINAL.

Claim Disposition

2. Claims 57-60 have been added. Claims 29, 39, 42 and 45 have been amended. Claims 1-60 are pending. Claims 1-34, 47-50 and 57-60 are under examination.

Oath/Declaration

3. The Oath/Declaration is defective because non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c) (see inventor Sampath). Correction is required.

See also claim 47 and the dependent claims thereto which have the same issues.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-34, 47-40 and 57-60 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. The claims are missing method steps critical or essential to the practice of the invention, but not included in the claim(s) thus, is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. There are many factors to be considered when determining whether there is sufficient evidence to support a

determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue. These factors include, but are not limited to:

I. Quantity of Experimentation Necessary:

The claims are directed to a method for repairing a defect locus in a nonarticular cartilage tissue and the method comprises providing an osteogenic protein...thereby inducing the formation of functional replacement (see for example claims 1 and 47). The specification describes the preparation of an implantable osteogenic device to provide the osteogenic protein. Note that the claim recites "providing an osteogenic protein" and does not recite how to achieve this result. Therefore, essential steps are missing from the claims. Thus, one of skill in the art would not be able to practice the claimed method without undue experimentation as essential method steps are missing to achieve the claimed objective. Claim 1 and claims with similar language needs to be amended to read *" A method for repairing a defect locus in a nonarticular cartilage tissue of a mammal, the method comprising: a) preparing an osteogenic device comprising an osteogenic protein in a biocompatible, bioresorbable carrier; and b) implanting said device into the defect locus, thereby inducing the formation of functional replacement cartilage tissue to repair said defect locus".* Note also that claim 47 does not recite an end point thus, the method is incomplete and would require undue experimentation.

II. Amount of direction or guidance presented:

The specification does not disclose one reasonable method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim. The claims are directed to a method and the only step recited broadly recites "providing". There is no indicia as to how to provide an osteogenic protein to produce the desired effect recited in the claim and the specification is not enabled for any apparatus, there is only support for implanting the protein in the disclosure. Therefore, absent adequate direction/guidance one of skill in the art would have to engage in undue experimentation to practice the full scope of the claims.

III. Presence or absence of working examples:

The examples provided do not support or exemplify the breath of the claims. The specification describes a osteogenic device, however, the claims read on any device known in the art with the method step of "providing".

IV. Nature of the Invention/State of the prior art and Relative skill of those in the art:

The invention is directed to a method for repairing a defect in a nonarticular cartilage tissue and the prior art describes implanting osteogenic proteins to repair the defect, however, the instant claims read on a broad spectrum of devices or apparatus as the claims do not recite how to provide the claimed protein to obtain the claimed effect.

VI. Predictability or unpredictability of the art/Breadth of the claims:

The breadth of the claims are very broad and encompass an unspecified amount of devices/apparatus to achieve the repair of the nonarticular cartilage which is not supported by the instant specification or the prior art, thus, the method as claimed is unpredictable.

Therefore, for all these reasons, the specification is not considered to be enabling for one skilled in the art to make and use the claimed invention commensurate in scope with the claims.

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-4, 7-11, 14-16, 25, 27, 47, 48, 57, 59 and 60 are rejected under 35 U.S.C. 102(b) as being anticipated by Luyten et al. (WO 96/143335, May 17, 1996).

Luyten et al. disclose cartilage-derived morphogenetic proteins having *in vivo* chondrogenic activity (CDMP-1 (GDF-5 or MP-52) and CDMP-2 (GDF-6)) in combination with a matrix, for example, freeze dried cartilage, collagen, hydorxyapatite, polylactic acid, polyethylene glycol, for the repair of cartilage such as subglottic stenosis, tracheomalacia, chondromalacia patellae, osteoarthritis, joint surface lesions (see claims 1-4, 7-11, 14-16, 25, 27,

47, 48, 57 of the instant application and page 2, lines 10-11; page 3 lines 4-23 and page 4 lines 21-36 of the reference). Luyten et al. teach that the CDMPs can be combined with a number of suitable carriers such as fibrin glue, cartilage grafts and collagens (see claim 14 of the instant specification and see page 19, lines 17-29). The reference also teach that the formulation can be administered via an injection (see claims 59,60). Therefore, the limitations of the claims are met by this reference because Luyten et al. teach the repair/formation of articular and nonarticular cartilage.

Claim Rejections - 35 U.S.C. § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103 (a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103 (c) and potential 35 U.S.C. 102 (f) or (g) prior art under 35 U.S.C. 103 (a).

8. Claims 1-6, 7-25, 27, 30-34 47, 48, 57 and 59-60 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Luyten et al. (WO 96/143335, May 17, 1996) taken with Celeste et al. (WO 95/126035, June 15, 1995) and Cui et al. (Ann. Otol. Rhinol. Laryngol. vol. 106, pages 326-328, 1997) .

Luyten et al. disclose cartilage-derived morphogenetic proteins having *in vivo* chondrogenic activity (CDMP-1 (GDF-5 or MP-52) and CDMP-2 (GDF-6)) in combination with a matrix, for example, freeze dried cartilage, collagen, hydorxyapatite, polylactic acid, polyethylene glycol, for the repair of cartilage such as subglottic stenosis, tracheomalacia, chondromalacia patellae, osteoarthritis, joint surface lesions (see claims 1-4, 7-11, 14-16, 25, 27, 47, 48, 57 of the instant application and page 2, lines 10-11; page 3 lines 4-23 and page 4 lines 21-36 of the reference). Luyten et al. teach that the CDMPs can be combined with a number of suitable carriers such as fibrin glue, cartilage grafts and collagens (see claim 14 of the instant specification and see page 19, lines 17-29). The reference also teach that the formulation can be administered via an injection (see claims 59,60). Luyten et al. do not teach the agent carboxymethylcellulose. However, Celeste et al. teach a pharmaceutically acceptable vehicle or carrier such as collagen, poly(lactic acid), polymers of lactic acid and poly(glycolic acid) and agents such as carboxymethylcellulose (see claims 1, 19, 25, page 16 and 19). Celeste et al. also

teach bone morphogenetic proteins useful in treatment of tendon or ligament defects such as induction and repair (see page 326) and that BMPs are useful in the formation of bone, cartilage and tendon, for example BMP-12 (see page 1 of the reference).

In addition, Cui et al. teach the repair of thyroid cartilage defect with bone morphogenetic protein by administering bBMPs for the replacement of lost laryngotracheal cartilage which results in new bone formation. Cui et al. teach that cartilage was initially formed but eventually gave room to new bone. Cui et al. differs from the claimed invention in that the replacement tissue which is formed is not functional cartilage, but bone (see claims 1-6, 8-18, 20-25, 27, 30-34). However, Cui et al. teach that the ideal way to a repair laryngotracheal defect is by inducing replacement cartilage growth.

Therefore, it would have been obvious to one of ordinary skill in the art to arrive at the claimed invention as a whole by combining the teachings of the references because all the references teach BMPs for inducing replacement growth of defects in cartilaginous tissue. One of ordinary skill in the art would be motivated to combine the references because Cui et al. teach that the ideal method for replacing lost laryngotracheal cartilage would be to induce growth of host replacement cartilage that would bridge an entire defect by means of a cartilage-inducing implant. Moreover, Cui et al. teach that laryngotracheal defect is a serious and difficult problem since it causes laryngotracheal stenosis and Celeste et al. teach that BMPs are useful for the induction or repair of bone, cartilage and tendon. Thus, the claimed invention was obvious to make and use at the time it was made and was *prima facie* obvious.

9. Claims 1-6, 8-25, 27 and 30-34 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Cui et al. (Ann. Otol. Rhinol. Laryngol. vol. 106, pages 326-328, 1997) in view of Celeste et al. (WO 95/126035, June 15, 1995).

Cui et al. teach the repair of thyroid cartilage defect with bone morphogenetic protein by administering bBMPs for the replacement of lost laryngotracheal cartilage which results in new bone formation. Cui et al. teach that cartilage was initially formed but eventually gave room to new bone. Cui et al. differs from the claimed invention in that the replacement tissue which is formed is not functional cartilage, but bone (see claims 1-6, 8-18, 20-25, 27, 30-34). However, Cui et al. teach that the ideal way to a repair laryngotracheal defect is by inducing replacement cartilage growth. In addition, Celeste et al. teach bone morphogenetic proteins useful in treatment of tendon or ligament defects such as induction and repair (see page 326). Celeste et al. teach that BMPs are useful in the formation of bone, cartilage and tendon, for example BMP-12 (see page 1 of the reference). Celeste et al. also teach a pharmaceutically acceptable vehicle or carrier such as collagen, poly(lactic acid), polymers of lactic acid and poly(glycolic acid) and agents such as carboxymethylcellulose (see claims 1, 19, 25, page 16 and 19).

Therefore, it would have been obvious to one of ordinary skill in the art to arrive at the claimed invention as a whole by combining the teachings of the references because both references teach BMPs for inducing replacement growth of defects in cartilaginous tissue. One of ordinary skill in the art would be motivated to combine the references because Cui et al. teach that the ideal method for replacing lost laryngotracheal cartilage would be to induce growth of

host replacement cartilage that would bridge an entire defect by means of a cartilage-inducing implant. Additionally, Cui et al. teach that laryngotracheal defect is a serious and difficult problem since it causes laryngotracheal stenosis. Moreover, Celeste et al. teach that BMPs are useful for the induction or repair of bone, cartilage and tendon. Thus, the claimed invention was obvious to make and use at the time it was made and was *prima facie* obvious.

Conclusion

10. No claims are allowable.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Hope A. Robinson whose telephone number is (703)308-6231. The Examiner can normally be reached on Monday - Friday from 9:00 A.M. to 6:30 P.M. (EST).

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor Christopher S.F. Low, can be reached at (703)308-2932.

Any inquiries of a general nature relating to this application should be directed to the Group Receptionist whose telephone number is (703)308-0196.

Papers related to this application may be submitted by facsimile transmission. The official fax phone number for Technology Center 1600 is (703) 308-2742. Please affix the Examiner's name on a cover sheet attached to your communication should you choose to fax your response. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989).

Hope A. Robinson, MS

Patent Examiner

Christopher S. F. Low

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